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TITLE: LIMITED TOXICITY AND MUTAGENICITY TESTING OF FIVE UNICHARGE PROPELLANT COMPOUNDS

SUBTITLE: Evaluation of Two Unicharge Propellants in the Acute Exposure Oral Toxicity in Rats

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Bis (2,2-dinitropropyl) acetal/formal (~50/50 mixture) ± diphenyl amine stabilizer (BDNPA/F±DPA) were tested for oral toxicity. Groups of ten rats per dose level were fasted and administered the test article orally by gavage. Animals were observed for clinical signs and mortality at 1 and 4 hours after dosing and once daily for 14 days. Based upon the results of these assays, the definitive acute oral LD_{50} (combined sexes) for BDNPA/F+DPA was determined to be 4791.1 mg/kg with 95% confidence limits of 3057.7 to 7507.2 mg/kg. The definitive acute oral LD_{50} for BDNPA/F-DPA was determined to be 3718.3 mg/kg with 95% confidence limits of 3311.2 to 4175.3 mg/kg.

14. SUBJECT TERMS

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Evaluation of Two Unicharge Propellants in the Acute Exposure Oral Toxicity in Rats

EXECUTIVE SUMMARY

In dose-range-finding studies, test articles bis-(2,2-dinitropropyl) acetal with diphenyl amine stabilizer and bis-(2,2-dinitropropyl) formal without diphenyl amine stablizer were orally administered to three groups of two rats (one/sex/group) per study at dose levels of 500, 2500 and 5000 mg/kg. Signs observed in both treatment groups included decreased activity, abnormal stance, abnormal gait, dyspnea and flaccid body tone. Poor grooming was also observed in the bis-(2,2-dinitropropyl) formal without diphenyl amine stablizer treated animals. None of the rats died at 500 mg/kg, two of two died at 2500 mg/kg and one of two died at 5000 mg/kg in the bis-(2,2-dinitropropyl) acetal with diphenyl amine stabilizer treated animals. Of the animals that received bis-(2,2-dinitropropyl) formal without diphenyl amine stabilizer, none of the rats died at 500 mg/kg and one of two died at 2500 mg/kg and two of two died at 5000 mg/kg. Based upon these results Definitive LD_{50}s were performed.

In a Definitive LD_{50}, bis-(2,2-dinitropropyl) acetal with diphenyl amine stabilizer was orally administered to five groups of ten rats (five males and five females per group), at dose levels of 1000, 1600, 2500, 3200 and 5000 mg/kg. Signs observed included decreased activity, abnormal gait, abnormal stance, dyspnea, poor grooming, ptosis, piloerection, decreased muscle tone and a discolored tail. There was an apparent increase in mean body weight in all surviving animals during the study. One of ten rats died at 1000 mg/kg. None of the rats died at 1600 mg/kg. Two of ten animals died at 2500 mg/kg. Three of ten animals died at 3200 mg/kg and seven of ten animals died at 5000 mg/kg. Necropsy of the animals that died on study revealed fluid-filled and/or distended intestines and stomachs, pale kidneys and a pale liver. No visible lesions were observed in any animal at terminal necropsy.

In a Definitive LD_{50}, bis-(2,2-dinitropropyl) formal without diphenyl amine stablizer was orally administered to six groups of ten rats (five males and five females per group) at dose levels of 1000, 1600, 2500, 3200, 4000 and 5000 mg/kg. Signs observed included decreased activity, abnormal stance, abnormal gait, dyspnea, decreased muscle tone, ptosis, poor grooming and tremors. There was an apparent increase in mean body weight in all surviving animals during the study. None of the animals died at 1000, 1600 and 2500 mg/kg. Two of ten animals died at 3200 mg/kg. Eight of ten animals died at 4000 mg/kg and nine of ten died at 5000 mg/kg. Necropsy of the animals that died on study revealed distended and/or fluid-filled intestines and stomachs. Terminal necropsy revealed an enlarged and hollow left kidney in one animal. No other visible lesions were observed in any of the remaining animals at terminal necropsy.

Based upon the observations made in the Acute Exposure Oral Toxicity studies in rats, the definitive acute oral LD_{50} (combined sexes) for bis-(2,2-dinitropropyl) acetal with diphenyl amine stabilizer was determined to be 4791.1 mg/kg with 95% confidence

limits of 3057.7 to 7507.2 mg/kg. The data generated to determine the LD_{50} for males and females separately did not lend itself to the statistical method employed. The definitive acute oral LD_{50} (combined sexes) for bis-(2,2-dinitropropyl) formal without diphenyl amine stablizer was determined to be 3718.3 mg/kg with 95% confidence limits of 3311.2 to 4175.3 mg/kg. The LD_{50} for males was determined to be 3911.6 mg/kg with 95% confidence limits of 3239.2 to 4723.5 mg/kg. The LD_{50} for females was determined to be 3479.3 mg/kg with 95% confidence of 3009.9 to 4021.8 mg/kg.

Evaluation of Two Unicharge Propellants
in the Acute Exposure Oral Toxicity in Rats

PH 402-US-001, 002-91

STUDY DESCRIPTION

Sponsor:	U.S. Army Medical Research and Development Laboratory Fort Detrick Frederick, MD 21702-5010
Testing Facility:	Pharmakon Research International, Inc. P.O. Box 609 Waverly, PA 18471
Test Facility Study Conduct S.O.P. No.:	PH-402
Study Numbers:	PH 402-US-001-91 PH 402-US-002-91
Purpose of the Study:	To determine the median lethal dose (LD_{50}), its statistical limits and slope using a single exposure and 14-day post-exposure observation period.
Ownership of the Study:	The sponsor owns the study. All raw data, analysis and reports are the property of the sponsor.
Study Monitor:	Major Nathaniel Powell, U.S. Army Medical Research and Development Laboratory
Study Director:	Victor T. Mallory, B.S., RLAT, Pharmakon Research International, Inc.
Technical Performance:	Thomas O'Neill, B.S., LAT, Kim DiLeo, B.S., LAT and Shirley Chappuis, A.S., AVT, LAT
Q.A.U. Responsible Personnel:	Leslie J. Pinnell, M.S.
Date Study Director Signed Protocols:	September 23, 1991

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Dates of Technical Performance:	Dose-Range-Finding PH 402-US-001-91 - October 21, 1991 through October 24, 1991 PH 402-US-002-91 - October 21, 1991 through October 24, 1991 Definitive LD_{50} PH 402-US-001-91 - November 4, 1991 through November 21, 1991 PH 402-US-002-91 - November 4, 1991 through November 27, 1991
Good Laboratory Practices Statement:	These studies were conducted in compliance with the Good Laboratory Practice Regulations. There were no deviations from the GLP Regulations which affected the quality or integrity of the study. Q.A.U. findings from the inspections conducted of this study and from the audit of the final report are documented and have been provided to the study director and the test facility management.
Statistics:	Statistics were calculated using Systat, Version 4.1, by Systat, Inc., Evanston, IL. LD_{50} determinations were calculated by the method of Litchfield and Wilcoxon via the Pharmacological Calculation System, Version 4.1.
Records Maintained:	All raw data, final report documentation and protocol will be maintained in the archives of Pharmakon Research International, Inc.
Recordings:	Standard Pharmakon Notebook
Notebook Reference:	Notebook #1539, pages 56-58, 60-71, 97-99, 101-114

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TEST ARTICLES

TEST ARTICLE	DESCRIPTION	LOT #	CAS #	DATE SUBMITTED
bis-(2,2-dinitropropyl) acetal/formal with diphenyl amine stabilizer (BDNPA/F+DPA)	yellow liquid	Set #1	5108-69-0	9/19/91
bis-(2,2-dinitropropyl) acetal/formal without diphenyl amine stabilizer (BDNPA/F-DPA)	yellow liquid	Set #2	5917-61-3	9/19/91

Analysis of Purity: The purity, identity, strength and stability of the test articles were the responsibility of the sponsor.

Stability: There was no apparent change in the physical appearance of the test articles during administration.

TEST SYSTEM

Species: Rat

Strain: Sprague Dawley

Suppliers (Sources): Charles River Laboratories, Inc., Wilmington, Massachusetts

Sex: Male and female

Age at Initiation: 8-10 weeks

Weight Range: Dose-Range-Finding - 160-190 grams
Definitive LD_{50} - 193-264 grams
The weight variation of animals used did not exceed ± 20 percent of the mean weight per sex.

No. on Study: PH 402-US-001-91 - Fifty (50) - (25 males and 25 females)
PH 402-US-002-91 - Sixty (60) - (30 males and 30 females)

Method and Justification for Randomization: Selection of rats based upon body weight.

Evaluation of Two Unicharge Propellants
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Acclimation Period:	Minimum of five (5) days
System of Identification:	Cage cards were marked with the study number, animal number, dose level and sex. Rats were ear tagged.

HUSBANDRY

Research Facility Registration:	U.S.D.A. Registration No. 23-R-107 under the Animal Welfare Act 74: SC 2131 et seq.
Animal Rooms:	Separate isolation by test system Light cycle - 12 hours light, 12 hours dark Temperature/Relative Humidity - Every attempt was made to maintain a temperature of 22°C ± 3°C (66-77°F) and a relative humidity of 30 to 70%. Any excursions outside the temperature or humidity ranges were of small magnitude and/or brief duration and did not adversely affect the validity of the study.
Housing:	Rats were housed individually in stainless steel ½" wire mesh cages, sized in accordance with the "Guide for the Care and Use of Laboratory Animals" of the Institute of Laboratory Animal Resources, National Research Council.
Sanitization:	Waste material was removed twice weekly. Cages and feeders were sanitized every two weeks.
Food:	Wayne Teklad Blox^{R}, ad libitum. Food was checked daily and added or replaced as needed. Feeders are designed to reduce soiling, bridging and scattering.
Food Analysis:	There were no contaminants that were reasonably expected to be present in the dietary material known to be capable of interfering with the purpose or conduct of the study.
Water:	Fresh tap water, ad libitum.
Water Analysis:	Water is monitored for contaminants at periodic intervals according to Standard Operating Procedure PH-018.

Evaluation of Two Unicharge Propellants
in the Acute Exposure Oral Toxicity in Rats
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METHODS

Rationale for Test System:	As per sponsor's request
Compound Preparation:	With the exception of the 5000 mg/kg dose levels, the test articles were weighed out and deionized water was added to achieve the appropriate dose. Tween 80 was also added to facilitate suspension. At 5000 mg/kg the test articles were dosed as received using specific gravity conversion.
Dose Administration:	Bis-(2,2-dinitropropyl) acetal with diphenyl amine stabilizer - 1000, 1600, 2500, 3200 and 5000 mg/kg Bis-(2,2-dinitropropyl) formal without diphenyl amine stablizer - 1000, 1600, 2500, 3200, 4000 and 5000 mg/kg
Rationale for Dose Selection:	Based upon the results of a dose-range-finding study.
Route of Administration:	The test articles were administered in a single dose by gavage, using a stainless steel gavage needle.
Rationale for Route of Administration:	According to the EPA Federal Register, Vol. 50, No. 188, Friday, September 27, 1985 and the Organization for Economic Co-operation and Development (OECD) Guidelines for testing chemicals, ISBN 92-64-12221-4, adopted by the council at the 535th meeting on May 12, 1981.
Frequency of Administration:	Once (1) per test article
No. of Animals Per Dose Group:	Ten (10)
Length of Studies:	Fourteen (14) days
Method of Study Performance:	Dose-Range-Finding Study In dose-range-finding studies, three groups of two rats (one male and one female per group) per study were fasted and administered neet material article at dose levels of 500, 2500 and 5000 mg/kg, orally by gavage. The rats were observed at approximately 1, ', 24, 48 and 72 hours after dosing for pharmacological and toxicological effects and mortality.

Definitive LD_{50}

In Definitive LD_{50}s, groups of ten rats (five males and five females per group) were fasted and administered neet material, at dose levels of 1000, 1600, 2500, 3200 and 5000 mg/kg [bis-(2,2-dinitropropyl) acetal with diphenyl amine stabilizer] and 1000, 1600, 2500, 3200, 4000 and 5000 mg/kg [bis-(2,2-dinitropropyl) formal without diphenyl amine stablizer], orally by gavage. The rats were observed at approximately 1, 4 and 24 hours after dosing and once daily through Day 14 for pharmacological and toxicological effects. Viability was checked daily. Body weights were recorded at study initiation, Days 7 and 14 or when found dead. All surviving rats were sacrificed by CO_2 inhalation and a gross necropsy performed.

RESULTS

Dose-Range-Finding Study

Signs observed in both treatment groups included decreased activity, abnormal stance, abnormal gait, dyspnea and flaccid body tone. Poor grooming was also observed in the bis-(2,2-dinitropropyl) formal without diphenyl amine stablizer treated animals. None of the rats died at 500 mg/kg, two of two died at 2500 mg/kg and one of two died at 5000 mg/kg in the bis-(2,2-dinitropropyl) acetal with diphenyl amine stabilizer treated animals. Of the animals that received bis-(2,2-dinitropropyl) formal without diphenyl amine stablizer, none of the rats died at 500 mg/kg, one of two died at 2500 mg/kg and two of two died at 5000 mg/kg. Based upon these results, Definitive LD_{50}s were performed.

Definitive LD_{50}

Signs observed in those animals receiving bis-(2,2-dinitropropyl) acetal with diphenyl amine stabilizer included decreased activity, abnormal gait, abnormal stance, dyspnea, poor grooming, ptosis, piloerection, decreased muscle tone and a discolored tail. There was an apparent increase in mean body weight in all surviving animals during the study. One of ten rats died at 1000 mg/kg. None of the rats died at 1600 mg/kg. Two of ten animals died at 2500 mg/kg, three of ten animals died at 3200 mg/kg and seven of ten died at 5000 mg/kg. Necropsy of the animals that died on study revealed fluid-filled and/or distended intestines and

stomachs, pale kidneys and a pale liver. No visible lesions were observed in any animal at terminal necropsy.

Signs observed in those animals receiving bis-(2,2-dinitropropyl) formal without diphenyl amine stablizer included decreased activity, abnormal stance, abnormal gait, dyspnea, decreased muscle tone, ptosis, poor grooming and tremors. There was an apparent increase in mean body weight in all surviving animals during the study. None of the animals died at 1000, 1600 and 2500 mg/kg. Two of ten animals died at 3200 mg/kg. Eight of ten died at 4000 mg/kg and nine of ten animals died at 5000 mg/kg. Necropsy of the animals that died on study revealed distended and/or fluid-filled intestines and stomachs. Terminal necropsy revealed an enlarged and hollow left kidney in one animal. No other visible lesions were observed in any of the remaining animals at terminal necropsy.

CONCLUSIONS

Based upon the observations made in the Acute Exposure Oral Toxicity studies in rats, the definitive acute oral LD_{50} (combined sexes) for bis-(2,2-dinitropropyl) acetal with diphenyl amine stabilizer was determined to be 4791.1 mg/kg with 95% confidence limits of 3057.7 to 7507.2 mg/kg. The data generated to determine the LD_{50} for males and females separately did not lend itself to the statistical method employed. The definitive acute oral LD_{50} (combined sexes) for bis-(2,2-dinitropropyl) formal without diphenyl amine stablizer was determined to be 3718.3 mg/kg with 95% confidence limits of 3311.2 to 4175.3 mg/kg. The LD_{50} for males was determined to be 3911.6 mg/kg with 95% confidence limits of 3239.2 to 4723.5 mg/kg. The LD_{50} for females was determined to be 3479.3 mg/kg with 95% confidence of 3009.9 to 4021.8 mg/kg.

Table I

Summary of Clinical Observations of Two Unicharge Propellants
in the Acute Exposure Oral Toxicity

PH 402-US-001, 002-91

Bis-(2,2-Dinitropropyl) Acetal with Diphenyl Amine Stabilizer

1000 mg/kg

Clinical Signs	Sex	Hours			Days												
		1	4	24	2	3	4	5	6	7	8	9	10	11	12	13	14
No signs	M	5	4	4	5	5	5	5	5	5	5	5	5	5	5	5	5
	F	5	3	3	4	4	4	4	4	4	4	4	4	4	4	4	4
Decreased Activity	M	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	2	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal Gait	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal Stance	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0

1600 mg/kg

Clinical Signs	Sex	Hours			Days												
		1	4	24	2	3	4	5	6	7	8	9	10	11	12	13	14
No signs	M	5	3	3	5	5	5	5	5	5	5	5	5	5	5	5	5
	F	5	3	3	5	5	5	5	5	5	5	5	5	5	5	5	5
Decreased Activity	M	0	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0

Table I (continued)

Summary of Clinical Observations of Two Unicharge Propellants
in the Acute Exposure Oral Toxicity

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Bis-(2,2-Dinitropropyl) Acetal with Diphenyl Amine Stabilizer

2500 mg/kg

Clinical Signs	Sex	Hours			Days													
		1	4	24	2	3	4	5	6	7	8	9	10	11	12	13	14
No signs	M	5	2	1	3	4	4	4	4	4	4	4	4	4	4	4	4
	F	5	1	1	3	3	4	4	4	4	4	4	4	4	4	4	4
Decreased Activity	M	0	3	4	2	1	1	1	1	1	1	0	0	0	0	0	0
	F	0	4	3	1	1	0	0	0	0	0	0	0	0	0	0	0
Poor Grooming	M	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0
	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ptosis	M	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal Gait	M	0	2	2	1	1	1	1	1	1	1	0	0	0	0	0	0
	F	0	1	2	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal Stance	M	0	2	2	1	1	1	1	1	1	1	0	0	0	0	0	0
	F	0	1	2	0	0	0	0	0	0	0	0	0	0	0	0	0
Dyspnea	M	0	0	0	0	1	1	1	1	1	1	0	0	0	0	0	0
	F	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Decreased Muscle Tone	M	0	0	0	0	0	1	1	1	1	1	0	0	0	0	0	0
	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection	M	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Discolored Tail (purple)	M	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0
	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Table I (continued)

Summary of Clinical Observations of Two Unicharge Propellants in the Acute Exposure Oral Toxicity

PH 402-US-001, 002-91

Bis-(2,2-Dinitropropyl) Acetal with Diphenyl Amine Stabilizer

3200 mg/kg

Clinical Signs	Sex	Hours			Days												
		1	4	24	2	3	4	5	6	7	8	9	10	11	12	13	14
No signs	M	5	2	0	1	1	1	1	3	3	3	3	3	3	3	3	3
	F	5	2	0	1	1	1	2	4	4	4	4	4	4	4	4	4
Decreased Activity	M	0	3	3	2	2	2	2	0	0	0	0	0	0	0	0	0
	F	0	3	4	3	3	3	2	0	0	0	0	0	0	0	0	0
Piloerection	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	0	0	0	2	2	0	0	0	0	0	0	0	0	0	0
Abnormal Gait	M	0	2	2	1	1	1	1	0	0	1	0	0	0	0	0	0
	F	0	1	2	1	1	1	1	0	0	0	0	0	0	0	0	0
Abnormal Stance	M	0	2	2	1	1	1	1	0	0	0	0	0	0	0	0	0
	F	0	1	2	1	1	1	1	0	0	0	0	0	0	0	0	0
Dyspnea	M	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0
	F	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0

Table I (continued)

Summary of Clinical Observations of Two Unicharge Propellants
in the Acute Exposure Oral Toxicity

PH 402-US-001, 002-91

Bis-(2,2-Dinitropropyl) Acetal with Diphenyl Amine Stabilizer

5000 mg/kg

Clinical Signs	Sex	Hours			Days												
		1	4	24	2	3	4	5	6	7	8	9	10	11	12	13	14
No signs	M	5	1	0	0	0	0	2	3	3	3	3	3	3	3	3	3
	F	5	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Decreased Activity	M	0	4	3	3	3	3	1	0	0	0	0	0	0	0	0	0
	F	0	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Abnormal Gait	M	0	2	3	3	3	3	1	0	0	1	0	0	0	0	0	0
	F	0	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Abnormal Stance	M	0	2	3	3	3	3	1	0	0	0	0	0	0	0	0	0
	F	0	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Dyspnea	M	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0
	F	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: Denotes all animals died on study

Table I (continued)

Summary of Clinical Observations of Two Unicharge Propellants
in the Acute Exposure Oral Toxicity

PH 402-US-001, 002-91

Bis-(2,2-Dinitropropyl) Formal without Diphenyl Amine Stablizer

1000 mg/kg

Clinical Signs	Sex	Hours			Days												
		1	4	24	2	3	4	5	6	7	8	9	10	11	12	13	14
No signs	M	5	4	4	4	5	5	5	5	5	5	5	5	5	5	5	5
	F	5	4	4	4	5	5	5	5	5	5	5	5	5	5	5	5
Decreased Activity	M	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0

1600 mg/kg

Clinical Signs	Sex	Hours			Days												
		1	4	24	2	3	4	5	6	7	8	9	10	11	12	13	14
No signs	M	5	3	3	4	5	5	5	5	5	5	5	5	5	5	5	5
	F	5	3	3	4	5	5	5	5	5	5	5	5	5	5	5	5
Decreased Activity	M	0	2	2	1	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	2	2	1	0	0	0	0	0	0	0	0	0	0	0	0

Table I (continued)

Summary of Clinical Observations of Two Unicharge Propellants
in the Acute Exposure Oral Toxicity

PH 402-US-001, 002-91

Bis-(2,2-Dinitropropyl) Formal without Diphenyl Amine Stablizer

2500 mg/kg

Clinical Signs	Sex	Hours			Days												
		1	4	24	2	3	4	5	6	7	8	9	10	11	12	13	14
No signs	M	5	5	4	4	5	5	5	5	5	5	5	5	5	5	5	5
	F	5	5	4	4	5	5	5	5	5	5	5	5	5	5	5	5
Decreased Activity	M	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
	F	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0

3200 mg/kg

Clinical Signs	Sex	Hours			Days												
		1	4	24	2	3	4	5	6	7	8	9	10	11	12	13	14
No signs	M	5	1	1	3	3	3	3	3	3	3	3	3	3	4	4	4
	F	5	1	2	2	2	2	2	4	4	4	4	4	4	4	4	4
Decreased Activity	M	0	4	3	1	1	1	1	1	1	1	1	1	1	0	0	0
	F	0	4	3	3	2	2	2	0	0	0	0	0	0	0	0	0
Abnormal Gait	M	0	3	3	1	1	1	1	1	1	1	0	0	0	0	0	0
	F	0	3	3	1	1	1	1	0	0	0	0	0	0	0	0	0
Abnormal Stance	M	0	3	3	1	1	1	1	1	1	1	0	0	0	0	0	0
	F	0	3	3	1	1	1	1	0	0	0	0	0	0	0	0	0
Dyspnea	M	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0
	F	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0
Decreased Muscle Tone	M	0	0	0	0	0	0	1	1	1	1	1	1	0	0	0	0
	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Table I (continued)

Summary of Clinical Observations of Two Unicharge Propellants
in the Acute Exposure Oral Toxicity

PH 402-US-001, 002-91

Bis-(2,2-Dinitropropyl) Formal without Diphenyl Amine Stablizer

4000 mg/kg

Clinical Signs	Sex	Hours			Days												
		1	4	24	2	3	4	5	6	7	8	9	10	11	12	13	14
No signs	M	5	0	0	0	0	0	1	1	2	2	2	2	2	2	2	2
	F	5	2	0	-	-	-	-	-	-	-	-	-	-	-	-	-
Decreased Activity	M	0	5	3	3	2	2	1	1	0	0	0	0	0	0	0	0
	F	0	3	2	-	-	-	-	-	-	-	-	-	-	-	-	-
Abnormal Gait	M	0	3	2	1	1	1	1	1	0	0	0	0	0	0	0	0
	F	0	2	2	-	-	-	-	-	-	-	-	-	-	-	-	-
Abnormal Stance	M	0	3	2	1	1	1	1	1	0	0	0	0	0	0	0	0
	F	0	2	2	-	-	-	-	-	-	-	-	-	-	-	-	-
Dyspnea	M	0	1	2	1	1	1	0	0	0	0	0	0	0	0	0	0
	F	0	1	2	-	-	-	-	-	-	-	-	-	-	-	-	-

-: Denotes all animals died on study

Table I (continued)

Summary of Clinical Observations of Two Unicharge Propellants
in the Acute Exposure Oral Toxicity

PH 402-US-001, 002-91

Bis-(2,2-Dinitropropyl) Formal without Diphenyl Amine Stablizer

5000 mg/kg

Clinical Signs	Sex	Hours			Days												
		1	4	24	2	3	4	5	6	7	8	9	10	11	12	13	14
No signs	M	5	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1
	F	5	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Decreased Activity	M	0	4	2	2	2	1	1	1	1	1	1	1	0	0	0	0
	F	0	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Abnormal Gait	M	0	3	2	2	2	1	1	1	1	1	0	0	0	0	0	0
	F	0	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Abnormal Stance	M	0	3	2	2	2	1	1	1	1	1	0	0	0	0	0	0
	F	0	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Dyspnea	M	0	2	2	2	2	1	1	0	0	0	0	0	0	0	0	0
	F	0	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Poor Grooming	M	0	0	0	2	2	1	1	0	0	0	0	0	0	0	0	0
	F	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Decreased Muscle Tone	M	0	0	0	0	1	1	1	1	1	1	0	0	0	0	0	0
	F	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Tremors	M	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
	F	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ptosis	M	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0
	F	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: Denotes all animals died on study

Table II

Summary of Mortality of Two Unicharge Propellants
in the Acute Exposure Oral Toxicity

PH 402-US-001, 002-91

Bis-(2,2-Dinitropropyl) Acetal with Diphenyl Amine Stabilizer

Dose (mg/kg)	Sex	No. of Rats	Days															Total Mortality
			0[a]	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
1000	M	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0/5
1000	F	5	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1/5
1600	M	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0/5
1600	F	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0/5
2500	M	5	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1/5
2500	F	5	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1/5
3200	M	5	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	2/5
3200	F	5	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1/5
5000	M	5	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	2/5
5000	F	5	0	5	-	-	-	-	-	-	-	-	-	-	-	-	-	5/5

a: Includes 1 and 4 hour observation periods
-: Denotes all animals died on study

Table II (continued)

Summary of Mortality of Two Unicharge Propellants
in the Acute Exposure Oral Toxicity

PH 402-US-001, 002-91

Bis-(2,2-Dinitropropyl) Formal without Diphenyl Amine Stablizer

Dose (mg/kg)	Sex	No. of Rats	Days														Total Mortality
			0[a]	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
1000	M	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0/5
1000	F	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0/5
1600	M	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0/5
1600	F	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0/5
2500	M	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0/5
2500	F	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0/5
3200	M	5	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1/5
3200	F	5	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1/5
4000	M	5	0	2	0	1	0	0	0	0	0	0	0	0	0	0	0	3/5
4000	F	5	0	4	1	-	-	-	-	-	-	-	-	-	-	-	-	5/5
5000	M	5	1	2	0	0	1	0	0	0	0	0	0	0	0	0	0	4/5
5000	F	5	0	5	-	-	-	-	-	-	-	-	-	-	-	-	-	5/5

a: Includes 1 and 4 hour observation periods
-: Denotes all animals died on study

Table III. Summary of Body Weights (g) of Two Unicharge Propellants in the Acute Exposure Oral Toxicity

PH 402-US-001, 002-91

Bis-(2,2-Dinitropropyl) Acetal with Diphenyl Amine Stabilizer

1000 mg/kg

Animal Number	Sex	Initial	Day 7	Final
5001	M	207	285	335
5002	M	215	275	317
5003	M	211	277	310
5004	M	209	258	306
5005	M	215	268	314
$\bar{x}$		211.4	272.6	316.4
S.D.		3.58	10.16	11.19
N		5	5	5
5006	F	193	-	-
5007	F	203	243	257
5008	F	195	239	258
5009	F	208	247	254
5010	F	206	216	255
$\bar{x}$		201.0	236.3	256.0
S.D.		6.67	13.89	1.83
N		5	4	4

1600 mg/kg

Animal Number	Sex	Initial	Day 7	Final
5011	M	218	279	328
5012	M	224	293	342
5013	M	226	302	359
5014	M	212	270	314
5015	M	211	263	306
$\bar{x}$		218.2	281.4	329.8
S.D.		6.80	16.07	21.34
N		5	5	5
5016	F	196	234	256
5017	F	196	228	247
5018	F	199	237	249
5019	F	218	270	299
5020	F	201	240	265
$\bar{x}$		202.0	241.8	263.2
S.D.		9.19	16.38	21.22
N		5	5	5

-: Denotes animal died on study

Table III. (cont'd) Summary of Body Weights (g) of Two Unicharge Propellants in the Acute Exposure Oral Toxicity

PH 402-US-001, 002-91

Bis-(2,2-Dinitropropyl) Acetal with Diphenyl Amine Stabilizer

2500 mg/kg

Animal Number	Sex	Initial	Day 7	Final
5021	M	255	131	-
5022	M	222	280	327
5023	M	208	275	326
5024	M	210	275	325
5025	M	220	279	329
$\bar{x}$		217.0	248.0	326.8
S.D.		7.55	65.45	1.71
N		5	5	4
5026	F	223	266	279
5027	F	206	238	258
5028	F	209	-	-
5029	F	211	251	274
5030	F	197	222	242
$\bar{x}$		209.2	244.3	263.3
S.D.		9.39	18.73	16.76
N		5	4	4

3200 mg/kg

Animal Number	Sex	Initial	Day 7	Final
5081	M	225	268	343
5082	M	231	266	308
5083	M	247	-	-
5084	M	259	-	-
5085	M	247	269	334
$\bar{x}$		247.8	267.7	328.3
S.D.		10.73	1.53	18.18
N		5	3	3
5086	F	211	240	259
5087	F	209	217	239
5088	F	208	223	253
5089	F	222	227	268
5090	F	210	-	-
$\bar{x}$		212.0	226.8	254.8
S.D.		5.70	9.74	12.18
N		5	4	4

-: Denotes animal died on study

Table III. (cont'd) Summary of Body Weights (g) of Two Unicharge Propellants in the Acute Exposure Oral Toxicity

PH 402-US-001, 002-91

Bis-(2,2-Dinitropropyl) Acetal with Diphenyl Amine Stabilizer

5000 mg/kg

Animal Number	Sex	Initial	Day 7	Final
5091	M	243	294	346
5092	M	227	252	298
5093	M	235	273	325
5094	M	240	-	-
5095	M	252	-	-
$\bar{x}$		239.4	273.0	323.0
S.D.		9.29	21.00	24.06
N		5	3	3
5096	F	217	-	-
5097	F	223	-	-
5098	F	212	-	-
5099	F	211	-	-
5100	F	229	-	-
$\bar{x}$		218.4	a	a
S.D.		7.60		
N		5	0	0

-: Denotes animal died on study
a: Not applicable

Table III. (cont'd) Summary of Body Weights (g) of Two Unicharge Propellants in the Acute Exposure Oral Toxicity

PH 402-US-001, 002-91

Bis-(2,2-Dinitropropyl) Formal without Diphenyl Amine Stablizer

1000 mg/kg

Animal Number	Sex	Initial	Day 7	Final
5031	M	210	257	311
5032	M	220	283	330
5033	M	205	263	297
5034	M	223	276	314
5035	M	208	261	309
$\bar{x}$		213.2	268.0	312.2
S.D.		7.86	11.00	11.86
N		5	5	5
5036	F	209	263	276
5037	F	198	231	249
5038	F	211	247	268
5039	F	202	235	250
5040	F	206	242	258
$\bar{x}$		205.2	243.6	260.2
S.D.		5.26	12.48	11.67
N		5	5	5

1600 mg/kg

Animal Number	Sex	Initial	Day 7	Final
5041	M	212	275	314
5042	M	213	271	320
5043	M	220	282	325
5044	M	212	277	324
5045	M	222	299	351
$\bar{x}$		215.8	280.8	326.8
S.D.		4.82	10.92	14.20
N		5	5	5
5046	F	213	247	274
5047	F	212	248	280
5048	F	210	244	267
5049	F	203	249	276
5050	F	196	240	258
$\bar{x}$		206.8	245.6	271.0
S.D.		7.19	3.65	8.66
N		5	5	5

Table III. (cont'd) Summary of Body Weights (g) of Two Unicharge Propellants in the Acute Exposure Oral Toxicity

PH 402-US-001, 002-91

Bis-(2,2-Dinitropropyl) Formal without Diphenyl Amine Stablizer

2500 mg/kg

Animal Number	Sex	Initial	Day 7	Final
5051	M	216	288	334
5052	M	228	278	322
5053	M	221	283	334
5054	M	220	286	341
5055	M	229	287	333
$\bar{x}$		222.8	284.4	332.8
S.D.		5.54	4.04	6.83
N		5	5	5
5056	F	204	235	250
5057	F	200	253	260
5058	F	204	235	248
5059	F	198	232	253
5060	F	209	243	268
$\bar{x}$		203.0	239.6	255.8
S.D.		4.24	8.53	8.20
N		5	5	5

3200 mg/kg

Animal Number	Sex	Initial	Day 7	Final
3181	M	238	-	-
3182	M	253	319	376
3183	M	235	215	293
3184	M	264	291	337
3185	M	263	282	329
$\bar{x}$		250.6	276.8	333.8
S.D.		13.61	44.08	34.05
N		5	4	4
3186	F	210	239	271
3187	F	220	231	257
3188	F	224	-	-
3189	F	209	244	279
3190	F	217	236	251
$\bar{x}$		216.0	237.5	264.5
S.D.		6.44	5.45	12.79
N		5	4	4

-: Denotes animal died on study

Table III. (cont'd) Summary of Body Weights (g) of Two Unicharge Propellants in the Acute Exposure Oral Toxicity

PH 402-US-001, 002-91

Bis-(2,2-Dinitropropyl) Formal without Diphenyl Amine Stablizer

4000 mg/kg

Animal Number	Sex	Initial	Day 7	Final
5061	M	229	-	-
5062	M	250	271	363
5063	M	225	277	328
5064	M	243	-	-
5065	M	233	-	-
$\bar{x}$		236.0	a	a
S.D.		10.30		
N		5	2	2
5066	F	219	-	-
5067	F	212	-	-
5068	F	212	-	-
5069	F	212	-	-
5070	F	215	-	-
$\bar{x}$		214.0	a	a
S.D.		3.08		
N		5	0	0

5000 mg/kg

Animal Number	Sex	Initial	Day 7	Final
5071	M	232	218	307
5072	M	235	-	-
5073	M	216	-	-
5074	M	233	-	-
5075	M	234	-	-
$\bar{x}$		230.0	a	a
S.D.		7.91		
N		5	1	1
5076	F	212	-	-
5077	F	215	-	-
5078	F	216	-	-
5079	F	204	-	-
5080	F	205	-	-
$\bar{x}$		210.4	a	a
S.D.		5.60		
N		5	0	0

-: Denotes animal died on study
a: Not applicable

Table IV

Necropsy Observations (Incidence Values) of Two Unicharge Propellants in the Acute Exposure Oral Toxicity

PH 402-US-001, 002-91

Bis-(2,2-Dinitropropyl) Acetal with Diphenyl Amine Stabilizer

1000 mg/kg

Observation	Interim Death Incidence		Terminal Necropsy Incidence	
	M	F	M	F
No visible lesions	-	0	5	4
Stomach fluid-filled	-	1	0	0

1600 mg/kg

Observation	Interim Death Incidence		Terminal Necropsy Incidence	
	M	F	M	F
No visible lesions	-	-	5	5

2500 mg/kg

Observation	Interim Death Incidence		Terminal Necropsy Incidence	
	M	F	M	F
No visible lesions	0	0	4	4
Stomach fluid-filled	0	1	0	0
Liver pale	1	0	0	0
Kidneys pale	1	0	0	0
Intestines distended	1	0	0	0
fluid-filled	1	0	0	0

-: Not applicable

Table IV (continued)

Necropsy Observations (Incidence Values) of Two Unicharge Propellants in the Acute Exposure Oral Toxicity

PH 402-US-001, 002-91

Bis-(2,2-Dinitropropyl) Acetal with Diphenyl Amine Stabilizer

3200 mg/kg

Observation	Interim Death Incidence		Terminal Necropsy Incidence	
	M	F	M	F
No visible lesions	0	0	3	4
Stomach				
distended	1	0	0	0
fluid-filled	1	0	0	0
Intestines				
distended	2	1	0	0
fluid-filled	2	1	0	0

5000 mg/kg

Observation	Interim Death Incidence		Terminal Necropsy Incidence	
	M	F	M	F
No visible lesions	0	0	3	-
Stomach				
distended	2	3	0	-
fluid-filled	2	3	0	-
Intestines				
distended	2	5	0	-
fluid-filled	2	5	0	-

-: Not applicable

Table IV (continued)

Necropsy Observations (Incidence Values) of Two Unicharge Propellants in the Acute Exposure Oral Toxicity

PH 402-US-001, 002-91

Bis-(2,2-Dinitropropyl) Formal without Diphenyl Amine Stablizer

1000 mg/kg

Observation	Interim Death Incidence		Terminal Necropsy Incidence	
	M	F	M	F
No visible lesions	-	-	5	5

1600 mg/kg

Observation	Interim Death Incidence		Terminal Necropsy Incidence	
	M	F	M	F
No visible lesions	-	-	5	5

2500 mg/kg

Observation	Interim Death Incidence		Terminal Necropsy Incidence	
	M	F	M	F
No visible lesions	-	-	5	5

-: Not applicable

Table IV (continued)

Necropsy Observations (Incidence Values) of Two Unicharge Propellants in the Acute Exposure Oral Toxicity

PH 402-US-001, 002-91

Bis-(2,2-Dinitropropyl) Formal without Diphenyl Amine Stablizer

3200 mg/kg

Observation	Interim Death Incidence		Terminal Necropsy Incidence	
	M	F	M	F
No visible lesions	0	0	4	3
Stomach				
distended	1	0	0	0
fluid-filled	1	0	0	0
Intestines				
fluid-filled	1	0	0	0
fluid-filled, red	0	1	0	0
Left kidney				
enlarged and hollow	0	0	0	1

4000 mg/kg

Observation	Interim Death Incidence		Terminal Necropsy Incidence	
	M	F	M	F
No visible lesions	0	0	2	-
Stomach				
distended	1	5	0	-
fluid-filled	2	4	0	-
Intestines				
distended	1	2	0	-
fluid-filled, red	1	0	0	-

-: Not applicable

Table IV (continued)

Necropsy Observations (Incidence Values) of Two Unicharge Propellants in the Acute Exposure Oral Toxicity

PH 402-US-001, 002-91

Bis-(2,2-Dinitropropyl) Formal without Diphenyl Amine Stablizer

5000 mg/kg

Observation	Interim Death Incidence		Terminal Necropsy Incidence	
	M	F	M	F
No visible lesions	0	0	3	-
Stomach				
distended	1	4	0	-
fluid-filled	3	5	0	-
Intestines				
distended	3	4	0	-
fluid-filled	1	2	0	-
fluid-filled, red	1	0	0	-

-: Not applicable

QUALITY ASSURANCE UNIT STATEMENT

Study Nos.: PH 402-US-001-91
PH 402-US-002-91

Study Director: Victor T. Mallory

The Quality Assurance Unit conducted the inspections listed below and reported the results to the study director and to management on the dates indicated.

The following inspections were performed:

Interval	Date
In Life Phase	11/4/91, 11/4/91
Necropsy Phase	11/21/91, 11/27/91
Reporting Phase	1/29/92

Date QAU Report Issued

To Study Director	To Management
1/29/91	1/29/92

Quality Assurance

Jan 29, 1992
Date

COMPLIANCE STATEMENT

This study was conducted in compliance with the Principles of Good Laboratory Practices (GLP) as promulgated by the following regulatory agencies.

Environmental Protection Agency as stated in the Federal Register, 40 CFR Parts 160 and 792.

Organization for Economic Co-operation and Development Guidelines for Testing Chemicals (OECD), ISBN 92-64-12221-4, adopted by the council at its 535th meeting on May 12, 1981.

U.S. Food and Drug Administration as stated in 58 CFR Part 21.

Study Nos.: PH 402-US-001-91
PH 402-US-002-91

To the best of my knowledge, this study was conducted in accordance with applicable Good Laboratory Practice regulations; there were no deviations from these regulations that impacted on study conclusions.

Study Director

Date May 29 1995